Abstract: PB2643

Title: LUSPATERCEPT IN MDS WITH RING SIDEROBLASTS: A REAL-LIFE EXPERIENCE

Abstract Type: Publication Only

Topic: Myelodysplastic syndromes - Clinical

Background:

The frontline treatment in low-risk anemic MDS (LR-MDS) patients is based on erythropoiesis stimulating agents (ESAs), however its efficacy is limited in terms of percentage of responsive patients and depth of response. Luspatercept is a recombinant fusion protein, which binds transforming growth factor-beta ligands in order to reduce SMAD2 and SMAD3 signaling, allowing erythroid maturation and erythroblastic differentiation. Recently, it has been approved for transfusion dependent anemia in MDS with ring sideroblast patients refractory or ineligible at ESAs therapy. Despite initial enthusiasms, luspatercept's response rates varies across studies, especially between clinical trials and real world data.

Aims:

We present a real-life experience in a cohort of transfusion-dependent MDS with ring sideroblast patients treated with Luspatecept.

Methods:

We collected data of 23 patients treated with Luspatercept from January 2021 to date. Patients were diagnosed with MDS with low blast count and SF3B1 mutation and/or ring sideroblasts (WHO 2022). Both Revised International Prognostic Score (IPSS R) and the Molecular International Prognostic Score (IPSS M) were calculated at diagnosis. All patients started Luspatecept because of an ESA-refractory transfusion dependent anaemia. Treatment response was evaluated at both 24 weeks and 1 year after the start of Luspatercept applying haematological response criteria proposed by the International Working Group 2018. Statistical analysis was performed with IBM SPSS 26

Results:

With a median follow-up of 19,4 months (range: 6,16-36,9), one patient discontinued treatment after 3 doses due to non-compliance, while 22 patients underwent treatment for 24 weeks and 16 for 1 year, without any evidence of side effects. Three patients discontinued treatment after 24 weeks due to loss of response (n=2) and disease progression to AML (n=1). At 24 weeks, 14 patients (63.5 %) achieved Hematological Improvement (HI), while 8 (36.5%) patients did not respond. At 1 year, 9 patients (56%) showed HI, while 7 (44%) did not respond. Overall, 8 (35 %) patients achieved transfusion independence at 24 weeks and 12 (51%) patients at one year of treatment. All non responders patients reached the maximum Luspatercept dose (1.75 mg/kg) and continued treatment up to 1 year, due to a reduction of Transfusion Burden (TB), not enough deep to meet 2018 IWG HI criteria. Fifteen patients are still in treatment, 1 stopped Luspatercept at 28 months due to progressive loss of response.

Applying Fisher's exact test, neither Transfusion Burden nor patient classification (IPSS R and IPSS M) have a statistically significant impact on the response totreatment, both at 24 weeks and at 1 year.However, we found that a low transfusion burden correlates positively with the achievement of transfusion independenceafter 24 weeks of treatment (p=0.002).There was no difference between the responder group and the non-responder group in terms of VAF of the SF3B1 clone, norany difference regardingthe number and type of concomitant mutations, assessed by NGS.

Summary/Conclusion:

Most patients took advantage from treatment with Luspatercept in our small series, achieving haematological

improvement with no evidence of side effects. Patients with a baseline low TB burden show a better response, in terms of transfusion independence, compared to high TB, as suggested in others cohorts. No other characteristics appeared to have a significant impact on transfusion dependence response. To confirm these findings and to identify predictive factors of response, a larger number of patients need to be included.

Total number of MDS-RS patients treated with Luspatercept	23
Age	
Years, median (range)	72 (52-89)
Sex, n (%)	
Male	13 (56)
Female	10 (44)
Cytogenetic, n	
Normal	18
Trisomy 8	2
Trisomy 14	1
Monosomy Y	1
del 20q	1
IPSS-R Classification, n (%)	
Very Low Risk	2 (9)
Low Risk	14 (61)
Intermediate Risk	7 (30)
Mutation status, detected by NGS	
SF3B1, n (%)	21 (91)
Vaf , %, median (range)	41 (25-46)
N co-mutation, median (range)	0 (0-2)
IPSS M Classification, n (%)	
Very Low Risk	2 (9)
Low Risk	15 (64)
Moderatly Low Risk	4 (18)
Intermediate Risk	2 (9)
Duration of EPO traitment before Luspatercept	
Months, median, range	30, 6-106
Transfusion burden sec. IWG 2018	
Low Trasfusion Burden, n (%)	7 (31)
High transfusion burden , n (%)	16 (69)

Keywords: Refractory anemia, MDS, Myelodysplasia, Myelodysplastic syndrome